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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,669	04/30/2001	Philippe Marliere	205907USOPCT	9510
22850 7590 12/01/2008 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER DUNSTON, JENNIFER ANN	
			ART UNIT	PAPER NUMBER
			1636	
			NOTIFICATION DATE	DELIVERY MODE
			12/01/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 09/830,669	<b>Applicant(s)</b> MARLIERE ET AL.	
	<b>Examiner</b> Jennifer Dunston, Ph.D.	<b>Art Unit</b> 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 86-104 and 106-134 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 86-102, 108-115 and 118 is/are allowed.
- 6) ☒ Claim(s) 103, 104, 107, 116, 117 and 119-134 is/are rejected.
- 7) ☒ Claim(s) 106 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/11/2008 has been entered.

Receipt is acknowledged of an amendment, filed 8/11/2008, in which claims 90, 103, 106 and 109 were amended, and claims 119-134 were newly added. Currently, claims 86-104 and 106-134 are pending and under consideration.

### ***Claim Objections***

Claim 123 is objected to because of the following informalities: (1) the phrase "selected from the groups consisting of" should be changed to "selected from the group consisting of" to improve the grammar of the claim; and (2) the word "cysteine" is misspelled. Appropriate correction is required.

Claim 124 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 124 recites, "the bacterial or yeast cell of claim 103, which is obtained by said method." However, claim 103 is drawn to the bacterial or yeast cell obtained

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by the recited method. In other words, both claims 103 and 124 claim the same bacterial or yeast cells.

Claim 125 is objected to because of the following informalities: the claim ends in two periods. Appropriate correction is required.

Claim 130 is objected to because of the following informalities: (1) the phrase "selected from the groups consisting of" should be changed to "selected from the group consisting of" to improve the grammar of the claim; and (2) the word "cysteine" is misspelled. Appropriate correction is required.

Claim 131 is objected to because of the following informalities: the word "cysteine" is misspelled. Appropriate correction is required.

Claim 132 is objected to because of the following informalities: the word "cysteine" is misspelled. Appropriate correction is required.

### ***Response to Arguments - Claim Objections***

The objection of claims 90 and 106 has been withdrawn in view of Applicant's amendment to the claims in the reply filed 8/11/2008.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claim 103, 104, 107, 116, 117 and 119-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection.

Claim 103 is vague and indefinite in that the metes and bounds of the phrase “wherein said cell comprises valyl-tRNA synthase including at least one mutation corresponding to K277Q, R223H, V276A or D2301” are unclear. The phrase is unclear in that the amino acid positions given in the claim are relative to an unnamed valyl-tRNA synthase. Different valyl-tRNA synthases are different lengths, and thus the numbered position of one conserved residue is not always the same regardless of the species selected. The specification describes those positions for *E. coli* valyl-tRNA synthase, and thus it would be remedial to indicate that the claimed positions correspond to K277Q, R223H, V276A or D2301 of *E. coli* valyl-tRNA synthase.

Claims 104, 107, 119-124, 131 and 133 depend from claim 103 and thus are indefinite for the same reasons applied to claim 103.

Claim 116 is vague and indefinite in that the metes and bounds of the structure of formula (I) are unclear. Formula (I) comprises two R groups: R<sub>1</sub> and R<sub>2</sub>. The claim recites, “wherein R<sub>1</sub> or R<sub>2</sub> represents radicals containing a functional group capable of reacting selectively.” Thus, the claim defines R<sub>1</sub> or R<sub>2</sub>. For the structure to be complete, both R<sub>1</sub> and R<sub>2</sub> must be defined. Because the complete structure of the compound is not defined by the claims, the metes and bounds are unclear. It would be remedial to amend the claim language to clearly indicate the structure of R<sub>1</sub> and R<sub>2</sub>.

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Claim 117 depends from claim 116 and is indefinite for the same reasons applied to claim 116.

Claim 125 is vague and indefinite in that the metes and bounds of the phrase “valyl-tRNA synthase including at least one mutation corresponding to K227Q, R223H, V276A or D230N” are unclear. The phrase is unclear in that the amino acid positions given in the claim are relative to an unnamed valyl-tRNA synthase. Different valyl-tRNA synthases are different lengths, and thus the numbered position of one conserved residue is not always the same regardless of the species selected. The specification describes those positions for *E. coli* valyl-tRNA synthase, and thus it would be remedial to indicate that the claimed positions correspond to K277Q, R223H, V276A or D2301 of *E. coli* valyl-tRNA synthase.

Claims 126-130, 132 and 134 depend from claim 125 and thus are indefinite for the same reasons applied to claim 125.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 103, 107 and 119-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

In the reply filed 8/11/2008, claim 103 was amended to limit the bacterial or yeast cell obtainable by the method of claim 86 to a cell that "comprises valyl-tRNA synthase including at least one mutation corresponding to K277Q, R223H, V276A or D230N, which allows said valyl-tRNA synthase to charge compounds that show steric resemblance to valine." The specification describes *E. coli* strains that contain one of the following mutations in the endogenous valyl-tRNA synthase gene: K277Q, R223H, V276A or D230N (e.g., pages 8, 24 and 31). At page 31, lines 23-27, the specification states, "Each one of these clones was shown to carry a different point mutation in the ValS gene, validating the selective screen as a means of diversifying the activity of valyl-tRNA synthetase in Escherichia coli." The specification does not disclose the corresponding mutations for other bacteria or yeast. The specification envisions identifying at least one mutation in an aminoacyl-tRNA synthetase gene of yeast or bacteria (e.g., page 6, lines 8-15). However, the mutations are defined relative to the corresponding wild-type gene (e.g., page 6, lines 8-15; page 6, lines 25-38) and not relative to the corresponding mutations in the *E. coli* valyl-tRNA synthetase gene. The as-filed specification provides general support for mutations in aminoacyl-tRNA synthetase genes of yeast and bacteria, and for the specific mutations in the valyl-tRNA synthetase gene of *E. coli* but does not provide support for the previously unnamed species of valyl-tRNA synthetase mutations in other bacteria or in yeast.

In the reply filed 8/11/2008, claim 125 was newly added. The claim is drawn to a bacterial or yeast cell which comprises a valyl-tRNA synthase including at least one mutation corresponding to K277Q, R223H, V276A or D230N, which allows said valyl-tRNA synthase to charge compounds that show steric resemblance to valine. The specification describes *E. coli* strains that contain one of the following mutations in the endogenous valyl-tRNA synthase gene:

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K277Q, R223H, V276A or D230N (e.g., pages 8, 24 and 31). At page 31, lines 23-27, the specification states, "Each one of these clones was shown to carry a different point mutation in the ValS gene, validating the selective screen as a means of diversifying the activity of valyl-tRNA synthetase in *Escherichia coli*." The specification does not disclose the corresponding mutations for other bacteria or yeast. The specification envisions identifying at least one mutation in an aminoacyl-tRNA synthetase gene of yeast or bacteria (e.g., page 6, lines 8-15). However, the mutations are defined relative to the corresponding wild-type gene (e.g., page 6, lines 8-15; page 6, lines 25-38) and not relative to the corresponding mutations in the *E. coli* valyl-tRNA synthetase gene. The as-filed specification provides general support for mutations in aminoacyl-tRNA synthetase genes of yeast and bacteria, and for the specific mutations in the valyl-tRNA synthetase gene of *E. coli* but does not provide support for the previously unnamed species of valyl-tRNA synthetase mutations in other bacteria or in yeast.

New claims 133 and 134 are drawn to specific species yeast that is *Saccharomyces cerevisiae*. The as-filed specification provides support for a genus of yeast cells obtained by the disclosed method (e.g., page 6, lines 19-24). The limitation of the yeast cell to *Saccharomyces cerevisiae* is new matter, because the original disclosure of a large genus does not provide support for a previously unnamed single species. The species of *Saccharomyces cerevisiae* is not specifically described by the as-filed specification.

The reply filed 8/11/2008 asserts that the claims are supported by the specification. Further, the response notes that the claims are directed to embodiments discussed in the paragraph bridging pages 4 and 5 of the Office action. The original specification has been thoroughly reviewed, and no support could be found for the amendments to claim 103, and



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claims that depend therefrom, and new claim 125, and claims that depend therefrom. The prior Office action indicates that *E. coli* strains deposited with the CNCM are described by the present specification, and these strains contain the mutations now claimed. However, the specification does not provide explicit or implicit support for the corresponding mutations in other bacteria or yeast valyl-tRNA synthase genes.

### ***Response to Arguments - 35 USC § 112***

The rejection of claim 109 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claim in the reply filed 8/11/2008.

Applicant's arguments, see page 12, filed 4/21/2008, and page 12, filed 8/11/2008, with respect to the rejection of claims 103, 104 and 107 under 35 U.S.C. 112, first paragraph, have been fully considered and are persuasive. The previous rejection of claims 103, 104 and 107 has been withdrawn.

### ***Citation of Pertinent Art***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Landés et al. A structure-based multiple sequence alignment of all class I aminoacyl-tRNA synthetases. *Biochimie* Vol. 77, pages 194-203, 1995. Figure 3 shows a multiple sequence alignment of ValRS from *E. coli*, *S. cerevisiae*, *N. crassa* mitochondrion, and *B. stearothermophilus*. The amino acid residues corresponding to K277Q, R223H, V276A or D230N of *E. coli* are conserved across all species disclosed by Landés et al.

***Conclusion***

Claims 86-102, 108-115 and 118 are allowed.

Claim 106 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner  
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/JD/

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Primary Examiner, Art Unit 1636